

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20089/S2

ADMINISTRATIVE DOCUMENTS

MEMORANDUM OF TELEPHONE CONVERSATION FEB 10 1992

NDA: 19,909/S-003 & S-004; 18-828/S-010 & S-012; 20-089/S-001

DATE: February 4, 1992

PRODUCT: Zovirax Suspension, Capsules and Tablets

SPONSOR: Burroughs Wellcome Co.

PARTICIPANTS: DAVDP
Donna Freeman, M.D. DSF 2/10/92
Dianne Murphy, M.D.
Carole Broadnax, CSO CB 2/10/92
and

Burroughs Wellcome
Sandra Lehrman, M.D.
Gray Davis, Ph.D.
Beverly Atwood, Pharm.D.
Elizabeth Andrews
Joan Drucker, M.D.
Karen Biron, Ph.D.
Nancy Bower
Dennis Troy, Marketing

SUBJECT: Follow-up to DAVDP's letter (NDA 19-909/S-003) to BW dated January 10, 1992, regarding labeling changes and requests for post-marketing studies of acyclovir suspension.

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Dr. Freeman initiated this call and had the following comments regarding BW's revised draft package insert dated January 23, 1992, and their draft response to post-marketing studies (copies attached).

Labeling - Attachment B

1. Please bold "within 24 hours" on lines three (3) and fifteen for ease of reading.
2. Dr. Freeman noted that it is confusing to sort out the results of the two (2) studies (e.g., patients ages 2 to 12 years and patients ages 13 to 18 years) referred to in the second paragraph (line 14). She stated that she will have to review specific sections of the NDA again to make sure these studies are properly represented in the labeling.

3. Dr Freeman commented that the material in lines 25 through 28 is in the NDA, but that inclusion of these results is new to the proposed labeling.

Labeling - Attachment C

4. Dr. Freeman requested that BW delete the first line of the **Herpes Zoster Infections** (line 23) and the **Chickenpox** (line 28) paragraphs. She commented that without the first sentence, the Herpes Zoster paragraph is fine. She asked BW to include a statement in the Chickenpox paragraph concerning their lack of information on the long term effects of treatment intervention on normal children with chickenpox.
5. From line 21 on, Dr. Freeman commented that BW should come up with phrasing that, in general, the disease is well tolerated and the degree of benefit from acyclovir is not dramatic. Dr. Lehrman stated that BW will put the phrase "one day" back in the labeling. Dr. Murphy commented that the greatest concern of the Advisory Committee is that the long term benefit of acyclovir is not known. Dr. Lehrman responded that the reason they have referred the reader back to the INDICATIONS AND USAGE section is so that they can judge for themselves what the differences are. Dr. Freeman stated that this may be difficult for the lay reader and that she is concerned that promotional materials are based on the way the label is written. Dr. Lehrman responded that BW will work on this.

BW's draft response to post-marketing studies

6. Regarding resistance, Dr. Freeman commented that virus isolated from a child pre-treatment is good and that the success of post-treatment isolation attempts may be so low as to not be worth the effort. She suggested that maybe virus could be obtained from peripheral blood. Dr. Biron responded that lesions are the most fertile culture area and that trying to obtain virus from blood will complicate things. She stated that she will need data from Dr. Balfour's study to determine how far into treatment the yield is good.

Dr. Freeman proposed the following:

- 1) Initiate a family study and look at the index case, and then specifically the exposed siblings. She commented that the drug will probably be used prophylactically even though it is not labeled for this.

- 2) Look at the sensitivity of isolates from the exposed siblings to monitor for insensitive virus if the drug is being used prophylactically. Such a study might be set up within a Health Maintenance Organization.
- 3) Why is the proposed four (4) arm treatment study being proposed in patients more than 12 years of age? Dr. Lehrman responded that she could not think of a prospective design for an exposure study.

BW concluded the conversation by offering to re-work the draft label again. They stated that the new draft would be arriving soon.

The conversation was cordial throughout.

cc: NDA ORIG. 19,909/S-003 & S-004; 18-828/S-010 & S-012;
20-089/S-001

HFD-530
HFD-530/ADMA/DMurphy
HFD-530/SMO/DFreeman/2-10-92
HFD-530/ASCSO/TDeCicco

HFD-530/CSO/CBroadnax/DRAFTED 2-6-92/EDIT 2-10-92